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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/555,102	07/17/2000	NICHOLAS THOMAS	PA9720	9263

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EXAMINER	
GABEL, GAILENE	
ART UNIT	PAPER NUMBER
1641	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/555,102	THOMAS, NICHOLAS	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-9 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-9 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/12/02 has been entered.

Amendment Entry

2. Applicant's amendment and response filed 4/12/02 in Paper No. 11 is acknowledged and has been entered. Claims 2, 4, and 10 have been cancelled. Claims 1, 6-8, and 11 have been amended. Accordingly, claims 1, 3, 5-9, and 11 are pending and are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112/102/103

3. The rejections of claims 2, 4, and 10 under 35 U.S.C. § 112, 102, or 103 are now moot in light of Applicant's cancellation of the claims.

4. In light of Applicant's amendment and arguments, the rejection of claims 1, 3, 5-7 and 9 under 35 U.S.C. 102(e) as being anticipated by Yamashita et al. (US 6,210,900), is hereby, withdrawn.

5. In light of Applicant's amendment and arguments, the rejection of claims 1, 3, and 5-9 under 35 U.S.C. 102(e) as being anticipated by Dower et al. (US 6,165,717), is hereby, withdrawn.

Rejections Maintained

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 3, 5-9, and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step a) is vague and indefinite in reciting, "said reagent being the same for all of said carrier beads and for all of said N populations" because it implies that the carrier beads and the N populations are 2 separate elements. Perhaps Applicant intends, "said reagent being the same for said carrier beads in all of said N populations".

In claim 1, step a), the term "the same" to make reference to the reagent bound to the carrier beads, is vague and indefinite because the term is a relative term that lacks a comparative basis for defining its metes and bounds. Does Applicant intend to

make reference to type, concentration, etc. of reagent coated in all the carrier beads in all of the N populations.

Claim 1, step d) is vague and indefinite in reciting, "providing in a fluid medium in each of said N different reaction vessels, additional reagents for performing an assay" because it is unclear as to whether the additional reagents contained in a fluid medium, are contained in each of the N different reaction vessels prior to addition of the carrier beads and the samples, or are subsequently dispensed into the N different reaction vessels. It is then further unclear as to how or when the step of "performing said assay" is effected, based on these limitations as set forth.

In claim 1, step d), the term "the same" to make reference to the additional reagents, is vague and indefinite because the term is a relative term that lacks a comparative basis for defining its metes and bounds. Does Applicant intend to make reference to type, concentration, etc. of additional reagents for each of the N different reaction vessels.

Claim 1, step d), lines 4-8, remains vague, indefinite, and confusing in reciting, "wherein one of said additional reagents or said reagent bound to the carrier beads, carries a signal moiety that is partitioned between said carrier beads and said fluid medium during the assay, in each of said N different reaction vessels", because it fails to specifically and distinctly define the functional cooperative relationship that exists between the reagents coated on the carrier beads, and the additional reagents provided for each of the N different reaction vessels so as to cause a signal moiety to be

partitioned between the carrier beads and the fluid medium during the assay. It is specifically unclear how the signal moiety is caused to be partitioned. Please clarify.

Claim 1, step f), parts i) and ii), are vague and indefinite because it is unclear how the signal moiety and the detectable label are measured and determined differentially, so as to provide a measure of the presence or absence of the compound being tested, concentration of the compound being tested, and biological activity of the compound to being tested, as well as an indication of the each of the samples containing the compound being tested. Specifically, step a) recites that the reagent bound to the carrier beads are the same, and in step d) the same additional reagents are provided in all of said N different reaction vessels. Please clarify.

Claim 6 is redundant and thus, confusing in reciting, "the reagent that is bound to said carrier bead, of the reagents recited in step d) is provided on said carrier beads, which are precoated with said reagent". Perhaps Applicant intends, "the reagent that is bound to said carrier beads in step a) are precoated on said carrier beads".

Claim 11 remains indefinite in reciting the term "identical", i.e. in color, form, the term "substantially identical", i.e. relative to what, and the term "additional reagents", i.e. encompassing lysing reagents and solubilizing reagents, because the terms are subjective and lack a comparative basis for defining their metes and bounds.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

7. Claim 11 is rejected under 35 U.S.C. 102(e) as being anticipated by Chandler et al. (US 5,981,180).

Chandler et al. disclose multiplexed analysis of samples each containing test compounds (analytes) (see column 7, lines 25-61). Chandler et al. disclose providing populations of carrier beads (beadsets or bead subsets) labeled with an appropriate reactant such as a biomolecule or a DNA sequence (see column 7, line 63 to column 6, line 9). Each population of beads is homogeneous and differing in at least one distinguishable parameter from other populations. Distinguishable parameters include size, shape, labels which have fluorescent emissions in more than one wavelength resulting from the presence of two or fluorochromes on the beads, etc. The classification parameter for each population is known and therefore the identity of each population can be verified using flow cytometry (see column 3, line 65 to column 4). Each bead population is coated with different reactants so as to bind or react and detect different compounds. For more quantitative analysis of compounds and biological

activity (kinetic studies), each population of beads may be coated with a same reactant but at different concentrations so as to produce populations varying in density of precoated reactant rather than type of reactant; thereby allowing a parameter to serve as an indicator of reactant identity or reactant density. Chandler et al. disclose incorporating the beads and reagents into a kit format.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1, 3, 5-7, and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chandler et al. (US 5,981,180) in view of Yamashita et al. (US 6,210,900).

Chandler et al. has been discussed supra. Chandler et al. differ from the instant invention in failing to disclose dispensing one of N populations of carrier beads having reagent bound thereto into N reaction vessels, adding thereto one of N samples into each reaction vessel, then further adding additional reagent for assay reaction; thereafter, the contents of each reaction vessel are combined into a single mixture for analysis using flow cytometry.

Yamashita et al. disclose a method for identifying test compounds having desired characteristics and identifying essential moieties in a lead structure which comprises preparing one or more encoded combinatorial libraries from a specified set of reaction sequences wherein the test compounds are tested for biological activity (pharmaceutical activity). Specifically, Yamashita et al. disclose providing populations of labeled (tagged) beads with fluorescent labeled identifiers attached thereto for encoding the combinatorial libraries (see Summary). Each population of beads is distinguishable from other populations by virtue of size, composition, fluorescent marker, and fluorescent label identifier. The identifier is a "coding" label attached to a population of beads by adding ratios of a fluorophore and a non-fluorophore or adding multiple different fluorophores in varying ratios (see column 3, lines 38-55). Yamashita et al. disclose that the number of readily distinguishable populations of beads correspond to the number of alternative variables in a registry. Yamashita et al. disclose dispensing an entirety of a population in a separate reaction vessel or well of a microtiter plate; beads usually are divided into populations of 1000 or more (see column 4, lines 16-37). Thereafter, appropriate reagents are added to each individual reaction vessel for reaction or assay to take place. After washing, the populations of beads are combined into a single mixture and subjected to flow cytometry for sorting (see column 4, lines 38-49). The compounds of the library can be tested using samples in a soluble receptor assay (see column 13, lines 1-7).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to have combined the reaction samples in the method of Chandler into

a single mixture for flow cytometric analysis as taught by Yamashita because Yamashita specifically taught that various encoded or tagged beads that have undergone reaction with a test compound, each individual bead having characteristic parameters, can be combined into a single mixture for flow cytometric analysis which allows for sorting, identification, and analysis based on the their characteristic parameters acquired after exposure with the corresponding compounds from the combinatorial libraries.

9. Claim 8 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chandler et al. (US 5,981,180) in view of Yamashita et al. (US 6,210,900) and in further view of Mandecki (US 5,641,634).

Chandler et al. and Yamashita et al. have been discussed supra. Chandler et al. and Yamashita et al. differ in failing to disclose that the beads populations are electronically labeled.

Mandecki et al. disclose a multiplex assay using electronically encoded carrier beads (solid phase particles associated with transponders) that are assigned a unique index number which can be retrieved by a scanner device at any time during an assay for a compound. According to Mandecki et al., the carrier beads are analyzed to detect a label indicative of a reaction or binding of the compound to the carrier bead such as fluorescence, color, or radioactivity. Analysis is then preceded or followed by the decoding of the index number from the transponder. Both analysis and decoding can be done using two different instruments : a fluorimeter and a scanner. Mandecki et al.

also disclose a kit for detecting biomolecular compounds in samples using carrier beads, assay vessels, coated labeled reagent (see columns 1-3).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to further electronically encode the populations of beads as disclosed by Mandecki so as to be an added "another" decipherable parameter in the bead populations in the method as taught by Chandler as modified by Yamashita because Mandecki specifically disclosed its applicability in multiplex assays such as the assay of Chandler. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the transponders of Mandecki into the method of Chandler as modified by Yamashita because Mandecki specifically disclosed their advantage in further detecting and differentiating increased number of analytes simultaneously in comparison to current multiplex assays.

Response to Arguments

10. Applicant's arguments filed 12/12/02 have been fully considered but they are not persuasive.

A) Applicant argues that the specific relationships between reagents, analytes, and signal moieties recited in the claims, vary based upon the particular application desired. Applicant contends that the claims should not be analyzed in a vacuum, but always in light of the specification. Applicant points out that in pages 7-15 of the specification two types of assays are discussed that are used in high-throughput screening applications; therefore, the specification provides ample guidance to one of

ordinary skill in the art to recognize the various structural and functional relationships between the reagents, i.e. carrier bound and additional reagents, carrier beads, compounds to be tested, and samples. Applicant submits that the claimed method is adaptable to a variety of assay applications.

In response, Applicant is requested to note that a requirement of 35 USC § 112 is that the specification conclude with the claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention. Accordingly, while Applicant is entitled to broad recitations of a claimed invention, the claim recitations should not preclude clarity and each claim should be able to stand on its own merits. In this case, indefiniteness appears to result from Applicant's intent to broadly encompass different separate assay applications in a base claim; thus, the different structural and functional cooperative relationships between the different separate elements of the assays rendered the assay claims indefinite and confusing. Alternatively, if it is Applicant's intent to claim two separate assay applications, it is suggested but not required that the two applications be recited and claimed separately if deemed necessary, to provide clarity and definiteness in claiming Applicant's invention.

11. For reasons aforementioned, no claims are allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (703)

305-0807. The examiner can normally be reached on Monday-Thursday from 6:30 AM - 4:00 PM and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (703) 308-3399. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Gailene R. Gabel
February 21, 2003

Christopher L. Chin

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
2/12/03